REMARKS

Claims 4-18 and 37 were pending in the application. Claims 4, 5, 6, 15-18, and 37 were canceled. Claims 38-44 were added. Support for the new claims can be found throughout the application as filed and for example, on pages 34-39. Upon entry of this amendment, claims 7-14 and 38-44 will be pending.

The foregoing amendments decrease the number of claims and issues. No new matter has been added.

Rejections under 35 U.S.C. § 112

Claims 4-18 and 37 were rejected under 35 U.S.C. §112, first paragraph, because allegedly

> the specification while being enabling for a method for preparing RNA-free cellular components in an *E. coli*, wherein the cellular component and RNaseI or RNaseA are produced by said *E. coli* cell and wherein RNase I or RNase A are expressed and secreted using an inducible or constitutive promoter, does not reasonably provide enablement for a method for preparing RNA-free cellular components wherein any RNase is expressed in any cell and wherein any RNase is expressed constitutively in the cytoplasm.

(Office Action, pages 3-4.) The Office further alleges that there is "no information as to which promoters can be used in any cell to produce RNases." (Office Action, page 5). As an initial matter, it is noted that claims 4,5,6, 15-18, and 37 have been canceled. Nonetheless, to the extent this rejection may be applied to the currently pending claims, Applicants submit the following arguments.

The present application provides sufficient guidance to enable one of ordinary skill in the art to make and use the invention. The Office alleges that, as written, the claims "encompass a method for preparing RNA-free cellular components wherein the RNase and the cellular component are both produced by the same microbial cell in the cytoplasm." The Office alleges that this type of coverage is not enabled because of what is discussed in Okorokov et al. and Zhu et al. Applicants respectfully disagree.

Okorokov and Zhu do not present ***any*** evidence that it would ***not*** be possible to prepare a RNA-free cellular component wherein the RNase is produced in the cytoplasm wherein the RNase's expression is induced. Okorokov discusses an efficient system for active bovine pancreatic ribonuclease expression in *E. coli*. Okorokov does not discuss the preparation of RNA-free cellular components as is claimed in the present application wherein the RNase expression is induced prior to isolating the cellular component. Putting the RNase under control of an inducible promoter allows the microbial cell to produce the cellular component for a sufficient amount of a time without the deleterious effects that may be caused by RNase expression in the cytoplasm. At a time determined by one of ordinary skill in the art, the RNase expression is induced subsequently to the cellular component production, so that when the cellular component is isolated, it is RNA-free.

Since neither the Okorokov reference nor the Zhu reference discusses preparing RNA-free cellular components, much less wherein the cellular component is made RNA-free by inducing expression of an RNase in the cytoplasm in the same cell, Applicants respectfully submit that these references do not show that the invention as claimed is not enabled.

As to the Office's allegation that there is no information as to which promoters can be used in any cell to produce RNases, Applicants respectfully disagree. First, the claims presently recite producing an RNA-free cellular component in a mirobial cell. The present application discusses promoters that can be used in microbial cells such as the *trp* promoter, T7 promoter, *tac promoter*, and other constitutive and inducible promoters. (see throughout the specification, and, for example, pages 21-22, 24, 26-27, 29, 32-33). Indeed, the specification discloses various promoters that can be used for any cell. Further, the types of promoters that can be used under different conditions to get the required results in microbial cells are well known to those of ordinary skill in the art . Therefore, the present application is completely enabled as to how to produce RNAses in microbial cells.

The Office also alleges that the present application is not enabled for practicing the claimed method with any RNase because it is allegedly "unclear that the use of specific RNases would also result in substantially RNA-free compositions as defined in the specification." (Office Action, page 5). Applicants respectfully disagree

The present application discusses both specific and non-specific RNases. For example, the specification discusses RNase T1, which preferentially cleaves 3' to G residues (see page 11, paragraph 0069). Thus, RNase T1 is specific to the 3' of G residues found in RNA. This is in contrast to a non-specific RNase, such as RNase I, which cleaves the phosphodiester bond of single stranded RNA 3' of any ribonucleoside (see page 11, paragraph 0069). Although RNase T1 is ***specific*** for the 3' side of G residues found in RNA, it is submitted that most, if not all, RNAs comprise enough G residues such that RNase T1 would cleave the RNA into small enough pieces such that any cellular component being prepared would be RNA-free. Applicants, however, invite the Examiner to submit a reference disclosing RNAs that would not be sufficiently degraded by such a specific RNase and, if no reference can be found, an affidavit under 37 C.F.R. §1.104(d)(2) substantiating this position. Furthermore, there is no requirement that the Applicants describe every RNase that could be used to prepare the RNA-free cellular components. It is within the knowledge of one of ordinary skill in the art to pick and choose RNases that are capable of degrading RNA sufficiently so that one can prepare an RNA-free cellular component. Whether the specific RNase is disclosed in the present application is not relevant. Rather, what is relevant are the teachings of the present application that enable one of skill in the art to prepare a RNA-free cellular component using ***any*** RNase wherein both the RNase and the cellular component are produced by the same cell.

Accordingly, the Applicants' present invention is completely enabled for one of ordinary skill in the art. Therefore, Applicants respectfully request that the rejection of the claims under 35 U.S.C. §112, first paragraph be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 4, 6-13, and 15-18 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable. As is clear from MPEP §2143, in order to establish a *prima facie* case of obviousness, the Examiner must first establish motivation to combine or modify the references.

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the

> reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

MPEP §2143. The Examiner, thus, cannot rely upon a reasonable expectation of success alone to establish motivation. Such reliance is improper.

Applicants maintain that the Office has employed inappropriate hindsight in maintaining this rejection. The Office simply has established no motivation to combine the references. Instead, in the office action, the Office merely attempted to remove a perceived obstacle to combining the references, i.e., and the presence of DNases. But removing an obstacle to combining is not the same as establishing the motivation to do so. The Office has not pointed to any disclosure in either reference, nor in the knowledge generally available to those skilled in the art, suggesting their combination.

Nonetheless, in view of the amendments made to the pending claims, the rejections under 35 U.S.C. § 103 are believed to be moot. None of the references cited by the Examiner alone or in combination suggest or discuss preparing an RNA-free cellular component wherein both the cellular component and the RNase are expressed and made from the ***same*** cell. Even if all the references were combined, a person of ordinary skill in the art would not be in possession of the claimed inventions. Notably, previous claim 5 was not rejected under 35 U.S.C. § 103 and thus it is believed that the rejection would not apply to the amended claims.

Accordingly, Applicants respectfully request the rejections under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-5593 to clarify any unresolved issues raised by this response.

Respectfully submitted,

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Doreen Yatko Trujillo
Registration No. 35,719

COZEN O'CONNOR, P.C.
1900 Market Street, 6th Floor
Philadelphia, PA 19103-3508
(215) 665-5593 - Telephone
(215) 701-2005 - Facsimile